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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
08/978,637	11/25/1997	ELAZAR RABBANI	ENZ-53(DIV5)	4643

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EXAMINER	
BOWMAN, AMY HUDSON	
ART UNIT	**PAPER NUMBER**
1635	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	04/04/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	08/978,637	RABBANI ET AL.	
	Examiner	Art Unit	
	Amy H. Bowman	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 December 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *See Continuation Sheet* is/are pending in the application.

4a) Of the above claim(s) *318-323* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *See Continuation Sheet* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *25 November 1997* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *10/27/03, 12/26/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Continuation of Disposition of Claims: Claims pending in the application are 245,248-251,253-255,260,264,265,268,270,272,284,288-290,296,299,303,304,308-313 and 318-324.

Continuation of Disposition of Claims: Claims rejected are 245,248-251,253-255,260,264,265,268,270,272,284,288-290,296,299,303,304,308-313 and 324.

DETAILED ACTION

Status of Application/Amendment/Claims

Applicant's response filed 12/26/2006 has been considered. Rejections and/or objections not reiterated from the previous office action mailed 4/21/2006 are hereby withdrawn. The following rejections and/or objections are either newly applied or are reiterated and are the only rejections and/or objections presently applied to the instant application.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114.

Applicant has added claim 324. Therefore, claims 245,248-251,253-255,260,264,265,268,270,272,284,288-290,296,299,303,304,308-313 and 318-324 are pending in the instant application. Claims 318-323 are withdrawn as being directed to non-elected inventions.

Applicant's amendments to the claims filed on 12/26/06, with respect to the rejection(s) of claim(s) under 35 U.S.C. 112, 2nd paragraph; 35 U.S.C. 101; and 35 U.S.C. 102 with regards to Izant et al. and Junker et al. have been fully considered and are persuasive. Therefore, the rejection has been withdrawn.

However, upon further consideration, a new ground(s) of rejection is made in view of the amendments filed on 12/6/06.

Sequence Compliance-Drawings

This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 because there are sequences in the drawings that do not contain a SEQ ID NO.

A complete response to this office action must correct the defects cited above regarding compliance with the sequence rules and a response to the action on the merits which follows.

The aforementioned instance of failure to comply is not intended as an exhaustive list of all such potential failures to comply in the instant application. Applicants are encouraged to thoroughly review the application to ensure that the entire application is in full compliance with all sequence rules. This requirement will not be held in abeyance.

Response to Applicants Arguments—35 U.S.C. 102(b)

Claims 245, 248-251, 253-255, 260, and 264, are rejected under 35 U.S.C. 102(b) as being anticipated by Bebenek et al. (J. Biol. Chem. 1989. 264(28)

16948-16956), and is repeated for the same reasons of record as set forth in the actions mailed on 7/29/05 and 4/21/06.

These claims were rejected over Bebenek et al., who teach that HIV virions reproduce imperfectly, which result in an average of five mutations per genome per round of replication. Essentially, the fact that Bebenek indicates that an average of five mutations occurs per round of replication is considered to indicate that the final product is mutated compared to the primary nucleic acid, which satisfies the limitation that the primary nucleic acid is not obtained from the secondary nucleic acid or gene product. Accordingly, Bebenek et al. teaches a primary nucleic acid construct, i.e. the HIV virion, which gives rise to a secondary nucleic acid, which in turn gives rise to a sense nucleic acid, which is the virus containing an average of five mutations, and is therefore considered to be different and thus not obtained with the primary nucleic acid construct. Clearly, since the sense nucleic acid contains promoters terminators etc., it is also considered to comprise a signal sequence, thus meeting all the limitations of the above claimed invention.

Applicant asserts that the mutations do not always occur in Bebenek and since the mutations do not occur 100% of the time, it would follow that a primary nucleic acid is sometimes obtained with the secondary nucleic acid or gene product. It is noted that the limitation "wherein said primary nucleic acid is not obtained with said secondary nucleic acid or gene product " is not given much weight in light of the rejection under 35 U.S.C. 112, 2nd paragraph explained below. The primary nucleic acid is not obtained with the secondary nucleic acid because the primary nucleic acid is the template.

However, for arguments sake, there are certainly instances wherein the primary nucleic acid construct of Bebenek et al. (the HIV virion) gives rise to a secondary nucleic acid, which in turn gives rise to a sense nucleic acid which is the virus containing an average of five mutations and would therefore not be obtained with the primary nucleic acid construct. Furthermore, it is well accepted that HIV mutates from its original form.

Applicant asserts that because the mutations do not always occur, the criteria for inherency has not been met and points to MPEP 2112. It is noted that MPEP 2113 states that the mere fact that a certain thing may result from a given set of circumstances is not sufficient. However, in the instant case Bebenek does not teach that mutations "may" occur. Bebenek et al. teaches that they *do* occur, at a rate of about 5 mutations per replication. While it may not be out of the realm of possibility to assert that HIV replication has occurred error-free at some point in time, this does not mitigate the fact that mutations have and do occur. Applicants have not provided any evidence or reasoning beyond mere assertion that refutes that Bebenek et al. teaches that mutations occur during HIV replication, and that such mutations are inherent to the process of HIV replication. The rejection is maintained therefore.

New Objections/Rejections

Claim rejections -- 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 245, 248-251, 253-255, 260, 264, 265, 308-311 and 324 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 265 recites the limitation "said antisense nucleic acid sequence". There is insufficient antecedent basis for this limitation in the claim.

Claim 308 recites the limitation "said specific nucleic acid sequence" in claim 299. There is insufficient antecedent basis for this limitation in the claim.

Claim 324 recites the limitation "said specific nucleic acid sequence" in claim 299. There is insufficient antecedent basis for this limitation in the claim. Claims 309-311 are rejected because they depend from claim 324.

Claim 245 recites, "wherein said primary nucleic acid is not obtained with said secondary nucleic acid or said gene product". It is not understood what is meant by "obtained with" in the context of the instant claim. The primary nucleic acid acts as a template for the synthesis of a secondary nucleic acid which acts as a template for the synthesis of a gene product, so it is not clear how the primary nucleic acid would be "obtained with" the secondary nucleic acid or gene product and the metes and bounds of the phrase "obtained with" are not understood. Claims 248-251, 253-255, 260 and 264 are rejected because they depend from claim 245.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the

art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 265, 268, 270, 272, 284, 288-290, and 296, are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. **THIS IS A NEW MATTER REJECTION.**

Claim 265 recites, "wherein said antisense nucleic acid sequence replaces sequences that participated in stem-loop formation in said snRNA". Although Figure 41 depicts a U1 with antisense sequence inserted, there is not support for molecules having each of the characteristics of claim 265 and an antisense nucleic acid sequence that replaces sequences that participated in stem-loop formation in any snRNA, as instantly recited. Claims 268, 270, 272, 284, 288-290, and 296 are rejected because they depend from claim 265.

Should applicant disagree, applicants are encouraged to point out with particularity by page and line number where such support might exist for each claim limitation added in the amended claims filed on 12/26/2006.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 299, 303, 304, 308, 312 and 313 are rejected under 35 U.S.C. 102(e) as being anticipated by Calabretta et al. (US 5,734,039).

The invention of the above claims is directed to an isolated multi-cassette nucleic acid construct comprising either more than one promoter or more than one initiator or both more than one promoter and more than one initiator, which upon insertion into a eukaryotic cell produces more than one specific nucleic acid, each such specific nucleic acid so produced being substantially nonhomologous with each other and being either complementary with a specific portion of one or more viral or cellular RNAs in a cell or binds to a specific viral or cellular protein, wherein each specific nucleic acid binds to different target nucleic acid sequences.

Calabretta et al. teach a composition for introducing two different antisense oligonucleotides specific for two different genes to a cell. Calabretta et al. teach a nucleic acid construct comprising a first promoter segment and a segment containing DNA of a cytoplasmic oncogene or proto-oncogene DNA, and a second promoter segment and a segment containing DNA of a nuclear oncogene or proto-oncogene. The DNA containing segments are in inverted orientation such that transcription of the DNA produces RNA complementary to the two mRNA transcripts of the two oncogene targets (see columns 8 and 9, for example). Calabretta et al. teach various modifications of the nucleic acids and teach means of delivery of the compositions.

Therefore, the instant invention is anticipated by Calabretta et al.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 299, 309, 310 and 324 are rejected under 35 U.S.C. 103(a) as being unpatentable over Calabretta et al. (US 5,734,039), in view of Binkley et al. (Nucleic Acids Research, 1995, Vol. 23, No. 16, pages 3198-3205).

The invention of the above claims is directed to an isolated multi-cassette nucleic acid construct comprising either more than one promoter or more than one initiator or both more than one promoter and more than one initiator, which upon insertion into a eukaryotic cell produces more than one specific nucleic acid, each such specific nucleic acid so produced being substantially nonhomologous with each other and being either complementary with a specific portion of one or more viral or cellular RNAs in a cell or binds to a specific viral or cellular protein, wherein each specific nucleic acid binds to different target nucleic acid sequences. The specific nucleic acid binds to a specific cellular protein comprising a localizing protein or a decoy protein.

Calabretta et al. teach a composition for introducing two different antisense oligonucleotides specific for two different genes to a cell. Calabretta et al. teach a nucleic acid construct comprising a first promoter segment and a segment containing

DNA of a cytoplasmic oncogene or proto-oncogene DNA, and a second promoter segment and a segment containing DNA of a nuclear oncogene or proto-oncogene. The DNA containing segments are in inverted orientation such that transcription of the DNA produces RNA complementary to the two mRNA transcripts of the two oncogene targets (see columns 8 and 9, for example). Calabretta et al. teach various modifications of the nucleic acids and teach means of delivery of the compositions.

Calabretta et al. do not teach nucleic acids that bind to cellular proteins.

Binkley et al. teach high affinity RNA ligands to human nerve growth factor (NGF), which is a protein that is essential for growth, differentiation and maintenance of neurons and has the ability to localize or attract NGF-sensitive growing axons. Binkley et al. teach that the SELEX procedure is a widely used technique for isolating, identifying, and characterizing RNAs with high specificity and affinity to proteins. Binkley et al. teach that specific RNA ligands to proteins can be isolated using SELEX.

It would have been obvious to incorporate RNA oligonucleotides that bind to proteins, as taught by Binkley et al. in place of the antisense oligonucleotides taught in the system of Calabretta et al.

One would have been motivated to incorporate RNA oligonucleotides that bind to proteins instead of the antisense oligonucleotides in the system of Calabretta et al. because Binkley et al. teach that high affinity RNA ligands to proteins, such as NGF that localizes NGF-sensitive growing axons, can be easily isolated using the SELEX procedure and teach that such RNAs may furnish useful diagnostic tools for the study of proteins. Since both types of nucleic acid oligonucleotides are used to determine

binding interactions, as evidenced by the teachings of Calabretta et al. and Binkley et al., one would have been motivated to express the RNA ligands taught by Binkley et al. in the system of Calabretta et al.

One would have a reasonable expectation of success given that each of the nucleic acid molecules were known to bind with target molecules in a sequence specific manner, as evidenced by Calabretta et al. and Binkley et al. One would have a reasonable expectation of success to express the protein binding RNA molecules of Binkley et al. in the dual system of Calabretta et al., with the advantage of producing two different binding molecules at once.

Thus in the absence of evidence to the contrary, the invention as a whole would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made.

Claims 299, 309-311 and 324 are rejected under 35 U.S.C. 103(a) as being unpatentable over Calabretta et al. (US 5,734,039), in view of Binkley et al. (Nucleic Acids Research, 1995, Vol. 23, No. 16, pages 3198-3205), as explained in the rejection under 35 U.S.C. 103(a) above, further in view of Craig et al. (WO 95/08635).

The invention of the above claims is directed to an isolated multi-cassette nucleic acid construct comprising either more than one promoter or more than one initiator or both more than one promoter and more than one initiator, which upon insertion into a eukaryotic cell produces more than one specific nucleic acid, each such specific nucleic acid so produced being substantially nonhomologous with each other

and being either complementary with a specific portion of one or more viral or cellular RNAs in a cell or binds to a specific viral or cellular protein, wherein each specific nucleic acid binds to different target nucleic acid sequences. The specific nucleic acid binds to a specific cellular protein comprising a localizing protein or a decoy protein.

Calabretta et. al. and Binkley et al. do not teach decoy proteins.

Craig et al. teach the expression of viral decoy proteins under the control of a locus control region and teach that decoy proteins act as antagonists to natural proteins involved in the replication of the HIV virus. Craig et al. teach that a decoy protein can be used as a mutant of a transactivator protein that is capable of binding to the transactivator-responsive site on the host or viral genome, yet is incapable of activating transcription (see pages 2 and 3, for example).

It would have been obvious to use the SELEX method to assay for RNA molecules that bind to a protein, as taught by Binkley et al. and to specifically use a decoy protein as the protein, as taught by Craig et al.

One would have been motivated to screen for resultant RNA aptamers against a decoy protein because Binkley et al. teach that high affinity RNA ligands to proteins can be easily isolated using the SELEX procedure and teach that such RNAs may furnish useful diagnostic tools for the study of proteins. Since Craig et al. teach that decoy proteins are proteins that are useful to serve as a mutant that is capable of binding to a preferred site but yet is incapable of activating transcription, one would have been motivated to use the SELEX method of Binkley et al. to identify RNA ligands to any known protein, such as the decoy proteins of Craig et al.

One would have a reasonable expectation of success given that Craig et al. teach the benefits of decoy proteins and Binkley et al. teach assaying for RNA aptamers to proteins and teach a method (SELEX) that is widely use to identify RNA molecules that bind to known proteins.

Thus in the absence of evidence to the contrary, the invention as a whole would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Amy H. Bowman whose telephone number is (571) 272-0755.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Doug Schultz can be reached on (571) 272-0763. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Amy H Bowman
Examiner
Art Unit 1635

AHB

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